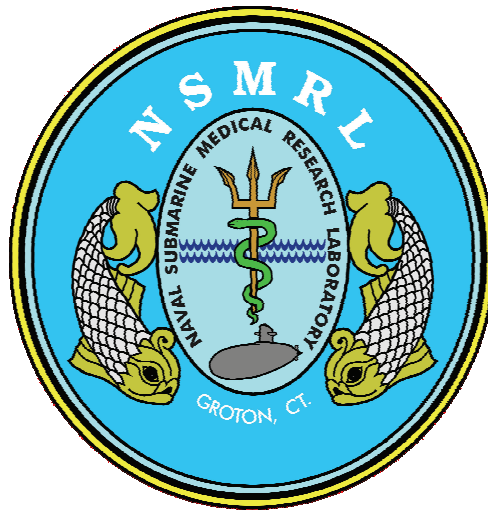


Naval Submarine Medical Research Laboratory

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An Analysis of the Cost-Effectiveness and Efficacy of Tobacco Cessation Aids

by

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ABSTRACT

Tobacco use costs the Department of Defense over one billion dollars in losses annually. The TRICARE formulary does not currently include smoking cessation medications, limiting availability to potentially helpful methods of cessation. This paper reviews the major approaches to cessation, both in relative success rates and cost effectiveness: abrupt cessation, nicotine replacement therapy, bupropion, and varenicline. Varenicline was shown to have the highest individual success rates with common but mild side-effects. Bupropion was determined the most cost effective medication, but it carries a risk of seizures and disqualifies nuclear field personnel. Nicotine replacement therapy, while slightly improving success rates, was shown to have the least cost-benefit and lowest efficacy. Counseling is recommended in adjunct of all pharmaceutical approaches. The paper concludes that varenicline is an effective and safe medication for smoking cessation and, despite its psychotropic status, should be considered for waiverable status for submariners and nuclear field service members.

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TABLE OF CONTENTS

ABSTRACT	iii
ACKNOWLEDGMENTS	iv
INTRODUCTION	1
The National Problem	1
The Navy's Problem	1
The Cost of Smoking in the Navy.....	2
BACKGROUND	2
Understanding the Addiction	2
Medications	3
METHODS	4
RESULTS	5
Abrupt Cessation/Cold-Turkey	5
NRT.....	6
Bupropion	8
Varenicline.....	8
Cost-benefit Analysis.....	10
DISCUSSION/CONCLUSIONS	11
REFERENCES	13

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INTRODUCTION

The National Problem

Nicotine addiction remains a prevalent form of drug abuse despite decades of anti-smoking campaigns. The health risks of smoking are well known, ranging from pulmonary infections to Chronic Obstructive Pulmonary Disease to lung cancer. Smoking kills 438,000 people per year in the U.S., half of them from cancer and the other half from a combination of cardiovascular diseases, stroke, emphysema, and other diseases.^{1,2} Annually, \$157 billion is lost to smoking-related health issues of the 44.5 million smokers in the U.S.³ A smoker costs the economy on average over \$3,500 per smoking year with the majority of the cost occurring as the smoker ages. TRICARE currently estimates that healthcare and related losses due to tobacco use costs the Department of Defense \$1.6 billion annually.⁴

The Navy's Problem

The percentage of smokers in the United States Navy, around 36-42%, is nearly double than that of the general population.^{5,6} In the general population, 70% of smokers have the desire to quit, and 42.5% have tried to quit in the past year; yet fewer than 7% who make the commitment to quit will remain smoke-free a year after their quit date.⁷ Obviously, these smokers desire to renounce their habit; yet nicotine's addicting qualities makes the task difficult.

The Navy should and does have a keen interest in promoting smoking prevention and cessation. The Chief of Naval Operations clearly states this goal (OPNAVINST 6100.2):

It is the Navy's policy to create an environment that supports abstinence and discourages the use of tobacco products, to create a healthy working environment, and to provide smokers with encouragement and professional assistance to stop smoking. The objective is to establish appropriate environmental protective measures to ensure a safe, healthy, unpolluted work and living environment. The Navy does not prohibit tobacco use, but employs a positive educational and awareness approach that is designed to provide the least disruption while improving the state of health and military readiness.⁸

Studies of smoking prevalence in the Navy are not encouraging. Not only does the Navy attract a higher percentage of smokers, enlisting somehow results in the development of the habit during basic training. While the national percentage of smokers remains at 20.9% and has remained relatively steady since 1990, 28% of incoming recruits are smokers. In a 1991 study, this number was shown to rise to 41% a year after initial entry. Nearly half of these new smokers started within their first two months in the Navy.⁹ In this light, it would seem appropriate for smoking prevention and cessation programs to be

ubiquitous. The majority of commands do provide educational materials for cessation, but surveys rate the effectiveness of these programs as “somewhat useful.”¹⁰

The Cost of Smoking in the Navy

Beyond the health hazards encountered by smokers, the Navy deals with the effects of smoking in realms beyond clinical medicine. Sailors who have never smoked are leaner and score higher on physical fitness tests than both current and former smokers. Former smokers score higher than current smokers and encounter fewer health problems while on active duty.^{7,11} A 2002 overview of the monetary costs of smoking revealed that smokers in the civilian workplace are absent 50% more and are 50% more likely to be hospitalized than non-smokers. Smokers also work on average 40 minutes less per day due to smoking breaks, becoming 1 full month of lost productivity per year.¹² Non-smoking enlisted men exhibit less chance-oriented personalities and report less stress than enlisted smokers.¹³ A study of female recruits found that daily smokers in the Navy receive reports indicating poorer job performance than non-smokers. Women who upon entry into service smoked at least once per day were more likely to not complete the full term of an enlistment, to have a less-than-honorable discharge, to receive a demotion, to desert, and/or not to reenlist.¹¹ Thus, the Navy sees both individual and organizational harms due to smoking.

This paper reviews the various approaches to smoking cessation while standardizing the results of various studies to “real-world” expectations. The success rates demonstrated by these approaches are used to create cost effectiveness figures. The safety and side effects of all medications are also included for consideration of introducing varenicline, the newest smoking cessation aid, for use in the submarine community.

BACKGROUND

Understanding the Addiction

Psychological and physical addiction to tobacco use develops quickly after initiation of a smoking habit. Nicotine, found in all tobacco products, meets all primary and additional criteria for an addicting substance as established by the Surgeon General.² More recently, the $\alpha_4\beta_2$ nicotinic acetylcholine receptor (nAChR) was identified as one of the major components involved in nicotine addiction. This ligand-gated membrane ion channel undergoes a prolonged activation by nicotine as compared to its endogenous agonist, acetylcholine.¹⁴ Activation of this receptor in the nucleus accumbens of the brain leads to dopamine release and eventually upregulation of the nAChR, as well as full gamma-aminobutyric acid (GABA) release.¹⁵ The extensive GABA release exhausts the inhibitory neurons, prolonging the effect of nicotine by shutting down the regulatory circuits. Activation of the central nervous mesolimbic dopamine system, then, is the primary known psychoactive mechanism of nicotine, producing both the emotional response and the tolerance so well documented clinically.

As nicotine is a psychotropic substance that produces dependence with sustained use, sudden discontinuation results in withdrawal symptoms. They include an intense craving for nicotine, increased tension or stress levels, irritability, headaches, difficulty in

concentrating, sleep disturbances (both drowsiness and insomnia), increased appetite, and weight gain.¹⁶ Urges to smoke are most intense and frequent in the first three days after the target quit date (TQD), the date set by the patient as the first attempted day of abstinence, and return for some time (*fig. 1*).¹⁷ All other symptoms usually return to baseline levels by day ten.¹⁸

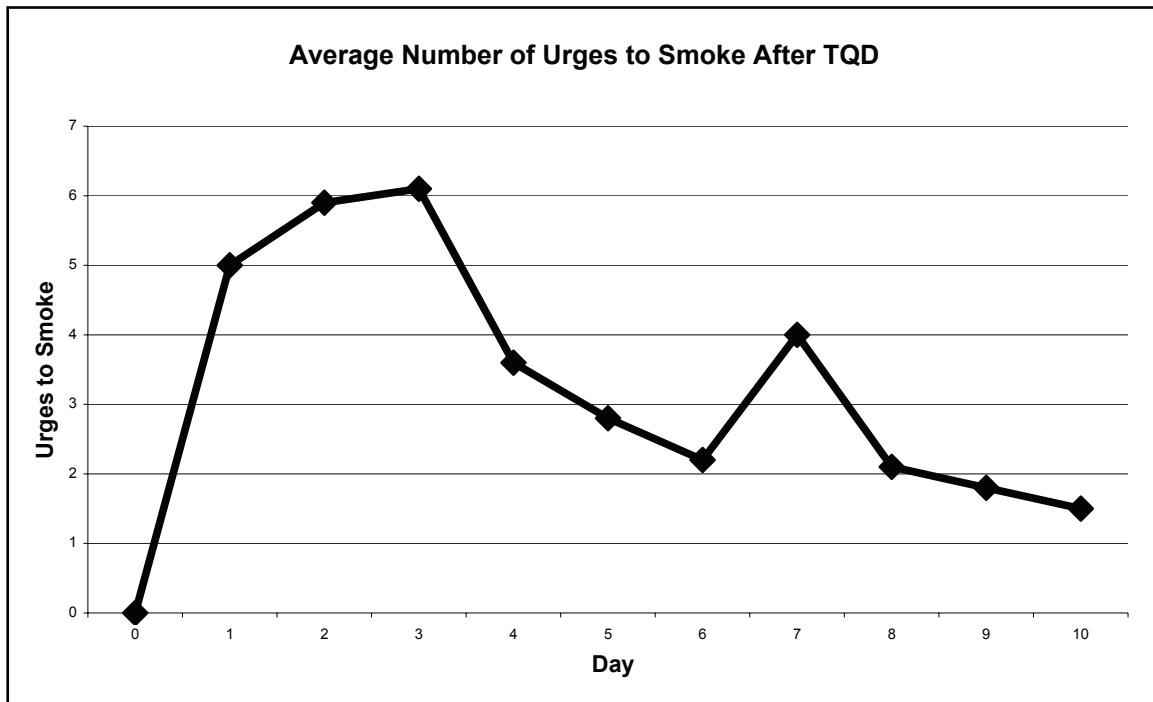


Figure 1. The average number of cravings, or urges to smoke, reported by subjects in a 1998 abrupt cessation study.¹⁷ Days 1-3, the physically dependent period, saw the greatest numbers. By day 10, only 1.5 urges to smoke were experienced by each patient.

Medications

In the 1980s, the first stop-smoking aid, nicotine gum, was made available through prescription. Some of these nicotine replacement therapy (NRT) medications, including gums (e.g., Nicorette[®]), transdermal patches (e.g., Nicoderm CQ[®]), and lozenges, are available over the counter (OTC) today. The nicotine inhaler, nasal spray, and sublingual tablet remain prescription only. All forms, regardless of their route, release nicotine at a controlled rate in order to reduce the urge to smoke.

The first non-nicotine medication approved for use in smoking cessation was bupropion hydrochloride, marketed as Zyban[®] by GlaxoSmithKline. Initially approved in 1984 as an atypical antidepressant under the name Wellbutrin[®], bupropion was removed from the market after a significant incidence of seizures was reported at the therapeutic dose. Burroughs-Wellcome, later Glaxo-Wellcome, reintroduced the drug at lower dosing in 1989. It was approved in 1997 as a smoking cessation aid. Bupropion acts as a reuptake inhibitor of both dopamine and norepinephrine. It is metabolized within the body into an

array of metabolites with differing activities, many of which effect the dopamine transporter and to a lesser degree norepinephrine reuptake.^{19,20} Studies have also shown noncompetitive inhibition of an nAChR, the $\alpha 3\beta 4$ receptor, may assist bupropion's ability to reduce the pleasurable response from smoking.²¹

The only non-nicotine medication developed specifically for cessation is varenicline, or Chantix[®], from Pfizer Inc. Varenicline binds with high affinity and high selectivity to the $\alpha 4\beta 2$ nAChR to produce both a partial agonistic and an antagonistic effect.²² As a competitive inhibitor, it blocks nicotine, a full agonist of the receptor. As a partial agonist, varenicline stimulates some dopamine release, although at a much reduced potency, about 13.4% that of acetylcholine.²³ This partial activation of the mesolimbic dopamine system combined with the blocking of nicotinic binding is the most likely mechanism for the compound's ability to reduce urges to smoke while reducing the emotional response usually derived from smoking.²⁴ The body does not significantly metabolize varenicline, and no clinically meaningful pharmacokinetic interactions have been identified.²⁵

The TRICARE formulary by policy does not currently include any medications expressly for smoking cessation. Smokers in the Navy can receive these medications by enrolling in a smoking cessation program, often provided by their local military medical treatment facility's wellness program. The smoking cessation program will have the local pharmacy special order NRT medications, which are then dispensed at no cost to the member. The formulary does include Wellbutrin[®], Wellbutrin SR[®], and Wellbutrin XL[®]. A physician can prescribe bupropion under these trade names, providing the prescription is written for an undisclosed diagnosis, not smoking cessation. Several Navy pharmacies are now independently considering the addition of varenicline to their formularies.

METHODS

We conducted a systematic review of the current literature describing tobacco cessation methods, success rates, and side effects. Both primary research and meta-analyses were examined, and all clinical trials in these sources were randomized, double-blinded, placebo-controlled trials unless otherwise noted in this paper. Costs of medication are according to the Naval Health Clinic New England, Naval Branch Health Clinic, Groton Pharmacy at Naval Submarine Base New London in Groton, Connecticut.

In comparing results across meta-analyses, the long-term quit rate (LTQR) at 52 weeks is used as the primary measure of efficacy. This term describes continuous abstinence after the TQD. The LTQR often includes a specified and limited number of days during the non-treatment phase up to which the patient can smoke but is still considered abstinent.

We selected the largest meta-analyses available concerning NRT and bupropion. Five major varenicline studies have been published to date; we have averaged the data from the four long-term studies of nearly 5,000 patients. American Cancer Society statistics and two literature review studies provided the abrupt cessation data. We also highlight

specific studies that directly compare one method to another. In all results, the 95% confidence intervals (CI) are the reported study values, weighted by trial size in the meta-analyses.

The cessation approaches reviewed often produce higher success rates than those normally encountered outside of controlled studies. Previous authors have attributed these inflated results to the heavy counseling, support, and financial assistance offered in clinical trials to specially selected participants, particularly in those studies funded or driven by manufacturers of the related medications. In an attempt to normalize the varying statistics, we employ two comparative methods in this paper in computing monetary costs.

First, to produce the average cost of a successful quit attempt, we divided the cost of medication for a standard or average regimen by the average success rates found using the above methods. Secondly, in order to compare varied or inflated data across differing studies, we also computed these figures using odds ratios (ORs) against placebo. By equating a controlled study placebo treatment with the known, functional “cold-turkey” quitting (which should be neurochemically equivalent) the OR for a medication was converted into an adjusted percentage relative to the difference between the study placebo quit rate and known cold-turkey quit rates. We refer to this value as *OR-adjusted*. This process is necessary to account for the confounders identified above. By using this approach, benefits in any individual study are at least partially corrected for and this allows for comparisons across multiple studies. The 95% CI is also reported. This cost analysis and OR-adjusted conversion are explained in the following example:

In a study where the medication costing \$100 for a full course has a 20% LTQR and placebo a 10% LTQR, 20 of 100 patients will succeed with the medication, or $1.00/0.20 = 5$. Thus, 1 of 5 patients will succeed in this example. These treatments cost $5 * \$100 = \500 in total, meaning \$500 is spent on average to produce one successful quit attempt, per the study. OR-adjustment takes the placebo rate of 0.10 in the study divided by the national abrupt cessation rate of 0.05, $0.10/0.05 = 2$. The 0.20 LTQR of the medication is divided by 2. $0.20/2 = 0.10$. Thus, a 10% “real-world” expected success rate. Now, 1 in 10 are successful. 10 patients at \$100/patient = \$1000 for one successful attempt on average. This number is the OR-adjusted cost.

RESULTS

Abrupt Cessation/Cold-Turkey

The LTQR at one year after the TQD is 5% nationally when attempted without extensive professional counseling or smoking cessation products.^{26,27} Nearly 50% of heavy smokers can achieve abstinence for 1-2 weeks, but the resumption of previous habits follows quickly after this period. This situation creates the typical scenario of the smoker who has “quit” 6-10 times before finally managing to stay smoke-free for a full year. Ex-smokers now outnumber smokers in the U.S., and 91% of them, 41 million people, quit using the “cold-turkey” approach.^{27,28}

The cost of abrupt cessation has a wide range of debated figures. While no purchases need be made, this oversimplification distorts the true costs. A primary care physician recommending quitting alone increases the chances of a successful quit attempt, but this interaction costs an indeterminate amount. If the patient attends professional counseling sessions, the patient must travel to the site; the counselor is paid for his or her time, and so on. Adding complexity, most ex-smokers did not attend an organized counseling session.²⁶ In this paper, the costs associated with “cold-turkey” are considered zero since they are non-exclusionary and too complex to report with any certainty. According to estimates from the Naval Branch Health Clinic, Groton, costs vary widely among programs sponsored by Navy medical treatment facilities, making estimates of cost to the Navy not useful for the purposes of this paper.

Those who do seek counseling as an adjunct to abrupt cessation show considerably higher success rates (*fig. 2*). Current clinical practice guidelines from the Surgeon General recommend counseling be used as part of any tobacco cessation therapy.²⁹

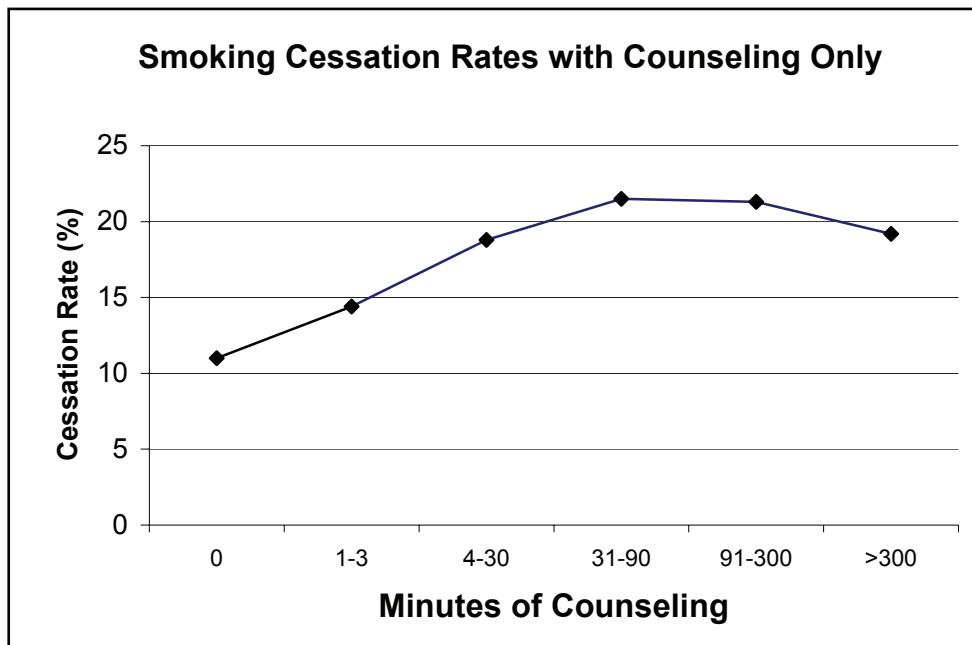


Figure 2. A comparison of counseling time to the LTQR. In all, 95 studies were reviewed, with the plateau of improvement appearing at 31-90 minutes. The x-axis is not a linear scale. Data from Fiore et al.²⁹

NRT

Initial studies boasted as high as a 44% cessation rate with NRT, making it an instant success statistically.³⁰ Further research has shown less dramatic results. A 2003 meta-analysis of NRT studies revealed an average effectiveness of 2.5 times that of placebo in controlled studies³¹ Real-world estimates continue to be highly debated, with most studies suggesting between 1.5 and 2.0 ORs and some as low as 3.0% abstinence rates at 6 months post-TQD, less than the abrupt cessation percentages.^{32,33} A 2002 review of

NRT effectiveness in clinical trials split ORs by delivery route from 1.61 to 2.27 (*tab. 1*).³⁴

Although NRT does reduce withdrawal symptoms, these medications also have side-effects in addition to the body's normal response to nicotine. The gum, for example, may cause skin irritation, dizziness, tachycardia, sleep disruptions, headaches, nausea, vomiting, myalgia, and muscle stiffness.³⁵ The packaging insert recommends use for no more than 3 months, yet some users will become dependent upon their therapy and continue nicotine replacement well beyond the suggested period.³⁶ A 2003 study found that 6.7% of initial gum purchases led to continued use beyond 6 months.³⁷ When compared to the average quit rate, this study suggests that up to half of patients who successfully quit using NRT may still be using the products beyond twice the maximum dosage period. Although nicotine is a psychotropic substance, NRT is approved for use by submariners and nuclear field service members.

Table 1. An OR comparison of 5 types of NRT. The 71 studies showed an average OR of 1.66 and statistically significant data for all but the sublingual lozenge delivery. Data from Woolacott et al.³⁴

<u>Route of NRT</u>	<u>Abstinence Rate</u>		<u>OR (95% CI)</u>	<u>Number of Studies</u>
	<u>NRT</u>	<u>Placebo</u>		
<i>Gum</i>	1,109/6,187	861/7,788	1.61 (1.45-1.78)	38
<i>Patch</i>	917/6,812	363/4,156	1.62 (1.42-1.84)	23
<i>Inhaler</i>	84/490	44/486	2.08 (1.43-3.04)	4
<i>Nasal Spray</i>	107/448	52/439	2.27 (1.61-3.20)	4
<i>Sublingual lozenge</i>	49/243	31/245	1.73 (1.07-2.80)	2
<i>Any</i>	2,266/14,181 16.0%	1351/13,114 10.3%	1.66 (1.54-1.79)	71

The costs associated with NRT can be less than smoking a pack of cigarettes per day. The least expensive NRT therapy, the transdermal patch, costs \$1.80 per day for 14 mg over 24 hours. A patient using a patch per day for 90 days requires \$162.00 worth of NRT. The 13.5% LTQR found in the above meta-analysis means 1 out of every 7.41 patients will successfully quit using patch NRT.³⁴ \$1200 is then needed to produce, on average, one successful quit. If 6.7% of initial purchases lead to continued use of NRT at 6 months and beyond, this figure increases to an estimated \$1280.

We now convert this figure into “real-world” expectations. The 13.5% LTQR for patch NRT in 23 studies of 10,968 total patients also found an 8.74% LTQR for placebo with an average OR of 1.62 (95% CI 1.42-1.84). Using the 5% national average estimates to adjust the NRT OR, 1 of every 12.3 patients (8.10% LTQR) would be expected to quit

using NRT. Dispensing \$2000 (95% CI \$1760-\$2280) worth of medication is then needed on average to produce a single successful attempt, ignoring the potential for continued purchases beyond 3 months. These results are summarized at the end of this section (*fig. 3*).

Bupropion

Bupropion was shown to have significantly higher success rates in its clinical trials than placebo for smoking cessation. Further research has confirmed its effectiveness, and the largest meta-analysis to date places its OR over placebo at 1.94 (95% CI 1.72 to 2.19), for a 13.4% LTQR.^{34,38} Studies directly comparing bupropion to NRT showed a higher LTQR with bupropion, 18% as compared to 10%.³⁹ When combined with NRT, studies have suggested that bupropion may have slightly higher success rates than seen with either therapy alone, although these results seem to vary unpredictably.⁴⁰

The side effects of bupropion are reported, in order of prevalence, as dry mouth, nausea, insomnia, tremor, diaphoresis, and tinnitus.⁴¹ As with all antidepressants, the box must include a suicide warning, as antidepressants have been found to increase suicidal behavior and suicidality in short-term studies of pediatric patients. This effect is still not known to extend into long-term studies or to affect adult patients. Independent studies of bupropion and several other antidepressants do not show a significantly different prevalence of suicidal thoughts or behavior from placebo.⁴² The risk of seizures depends upon dosage: 0.1% at 100-300 mg daily, 0.4% at 300-450 mg, and 2% at 600 mg.⁴³ Cessation success rates are also dose dependent but begin to plateau at 300 mg daily.⁴⁴ Dosage for tobacco withdrawal symptoms starts at 150 mg daily for three days followed by 7-12 weeks of 150 mg twice daily. Bupropion's status as a psychotropic medication prevents its use by submariners for beyond 30 days. It is automatically disqualifying for one year with an opportunity for waiver thereafter if it is taken beyond 30 days or for a use other than smoking cessation. For nuclear workers, any use is disqualifying for at least one year.⁴⁵

Generic bupropion costs \$0.86 per day for 150 mg twice daily. For a full course, including the initial titration, this comes to \$72.24 for 12 weeks. Using the above meta-analysis average of 13.9% LTQR, 1 smoker out of 7.19 will succeed with bupropion. \$520 is then needed for one successful patient. The OR-converted value suggests 1 out of 9.70 patients (10.3%) will quit. \$701 (95% CI \$660-\$840) is spent on medication for these attempts to produce the single successful patient.

Varenicline

Phase II and III clinical trials of varenicline showed significantly higher cessation rates than placebo. The pooled data of four long-term studies shows an LTQR of 21.9% vs. 8.4% for placebo (OR of 2.96, 95% CI 2.12–4.12). Two of these studies also compared the drug to bupropion, which was 16.1% effective at 52 weeks (varenicline:bupropion OR of 1.36). The study completion rates for these studies were 60% for varenicline, 56% for bupropion, and 54% for placebo.^{46,47} If the study dropouts are considered to all remain

smokers at 52 weeks, the abstinence rates become 13.1%, 9.01%, and 4.5% for varenicline, bupropion, and placebo, respectively. The 4.5% abstinence rate for placebo in these calculations matches closely the estimated national “cold-turkey” LTQR of approximately 5%.

It should be noted that the clinical trials for varenicline have come under some scrutiny for several possible experimental flaws. Blinding failures may have biased some results. Nearly all of the participants had attempted to quit at least once before enrolling, so most would be familiar with their withdrawal syndromes when given placebo. Similarly constructed trials of NRT were shown in a 2004 review to have serious blinding failures, where two-thirds of the patients receiving placebo accurately predicted not receiving the actual medications.⁴⁸ Patients were also allowed to use NRT during the non-treatment follow-up period (weeks 13-52 in the four studies). Finally, counseling in the two largest studies included 160 minutes of provider-to-patient counseling time (16 sessions of 10 minutes each) plus 8 telephone calls.^{49,50} This amount of counseling would be predicted to result in a 28.4% quit rate as shown above in *fig. 2*. Studies of varenicline’s effectiveness without the impact of heavy amounts of counseling have not yet been published.

The most commonly reported side effect of varenicline in clinical trials was nausea, which occurred in 30% of subjects taking 1 mg twice daily vs. 10% with placebo. For subjects taking 0.5 mg twice daily, the incidence was 16% vs. 11% with placebo. Other common side effects (>5% incidence and at least twice the rate seen with placebo) were insomnia, constipation, flatulence, and vomiting. For these other side effects, discontinuation rates were similar to placebo. The discontinuation rate due to adverse events in clinical trials was 12% vs. 10% for placebo in the 3-month-long treatment phases, a non-significant increase.²⁶ Serious adverse events encountered in the three long-term studies were similar in number between varenicline and placebo groups. Of the 4,500 patients exposed to varenicline in all safety studies, 3 deaths were reported, none of which was found linked to the medication: a patient previously diagnosed with depression who did not disclose his illness to researchers died of suicide 27 days after finishing the treatment phase; a patient died of lung cancer 19 days after finishing treatment; and a patient who dis-enrolled on day 25 of open label treatment died of a rectal sarcoma 197 days later.⁵¹ Two deaths were reported in the 1,500 other subjects not receiving varenicline, both not attributable to medication. As opposed to many other psychotropic medications, varenicline was not found to produce sedation, disinhibition, depression, or a stimulatory effect.^{49,51,52}

Dosing begins with 3 days of 0.5 mg daily titrated to 3 days of 0.5 mg twice daily, followed by 1 mg twice daily for the remainder of 12 weeks. Recommendations do allow for a reduction in dose if the patient cannot tolerate the full dose. An additional 12 weeks may be used to increase the chances of maintaining abstinence in those individuals who are abstinent after the initial 12 weeks. In a study of open label use for 12 weeks followed by randomization and double-blinded, placebo-controlled use by the remaining abstinent subjects, of the 64% (n=1236) who qualified for the second phase, 70% remained abstinent in the second 12-week period vs. 50% for placebo.⁵⁰

A 12-week treatment of varenicline, available by brand name only, is \$190.82. Using a success rate of 21.9% (OR of 2.96, 95% CI 2.12-4.12), the average for the four clinical trials, 1 of 4.57 patients will achieve long-term abstinence. These patients require \$871 worth of medication for each successful cessation. Using the OR-adjusted value, 1 of 6.76 will succeed, requiring \$1290 (95% CI \$926-\$1800).

Cost-benefit Analysis

A summary of the reported cost figures, derived from the meta-analyses, and the OR-adjusted values appears in the following (fig. 3). A recent study predicting the expected savings through employer-funded cessation programs and medications also found that both varenicline and bupropion save the employer money after only one year.⁵³

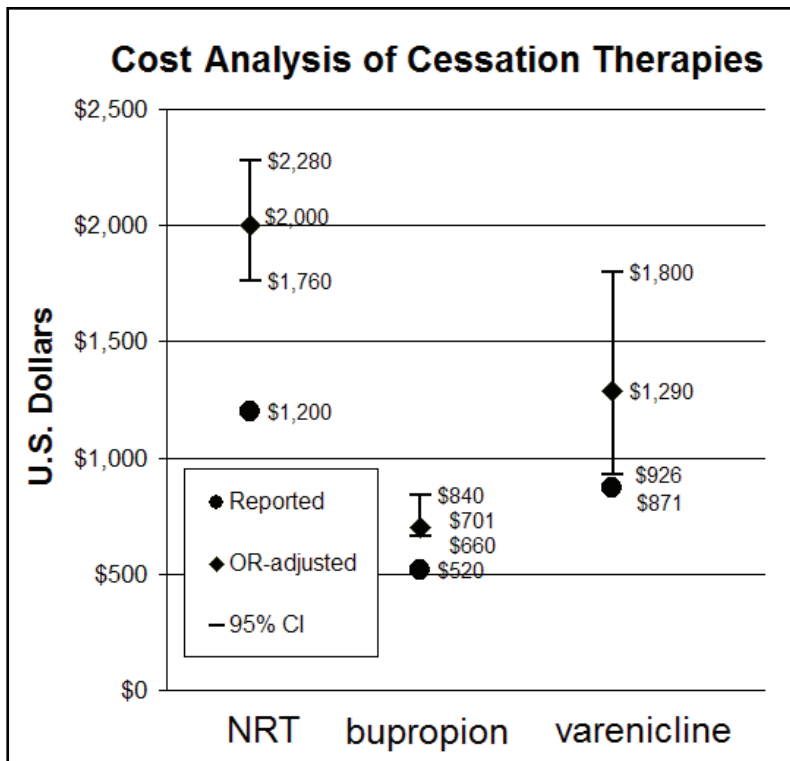


Figure 3. A summary of medication costs associated with three therapies to produce 1 successful abstinent smoker at 1 year post-TQD. The reported values were computed using large meta-analyses. The OR-adjusted values are these reported values after adjustment for “real-world” conditions.

DISCUSSION/CONCLUSIONS

The high prevalence of smoking in the Navy suggests the current smoking cessation strategies are not outpacing the influx of new smokers as recruits and the generation of smokers in the fleet. Encouraging these smokers to quit provides individual health improvements and monetary savings as well as the organizational-level benefits of increased productivity and reduction in healthcare cost. Given the highly addictive nature of nicotine, this goal remains elusive for most smokers in each single attempt. Nevertheless, the vast numbers of ex-smokers nationwide prove that quitting is feasible.

The first and overriding conclusion from the data suggests that counseling is at least as effective as medications. Only 1-3 minutes of counseling by a professional produces a 30% increase in the baseline success rate. A physician who recommends quitting improves the patient's odds of a successful attempt. At 31-90 minutes of counseling, which a tobacco cessation program can accomplish through a few short visits, the LTQR rate doubles. Although exact costs will vary from program to program, group counseling sessions already exist at most bases. Every clinical trial reviewed above included counseling in addition to medications, and to expect a therapy to produce similar results, counseling must be included in treatment plans.

Varenicline produces higher success rates than either NRT or bupropion, both of which are more efficacious than abrupt cessation. After OR-adjusting the results seen in controlled clinical trials that included large amounts of counseling, varenicline still maintains its higher LTQR. These values also match the results obtained by considering all study dropouts to resume smoking, a reasonable assumption in an intent-to-treat clinical trial involving an addictive substance. By reducing the amount of dopamine and GABA released by nicotine and acting as only a partial agonist, varenicline has an intrinsically reduced psychotropic effect for smokers. Massive clinical trials have demonstrated varenicline's efficacy and good safety profile.

From an organizational standpoint, bupropion is the most cost-effective medication for smoking cessation, followed by varenicline. Abrupt cessation with counseling also shows relatively high success rates, although costs for this method could not be computed as distinctly as medications. The cost of treatment with bupropion, varenicline, or NRT to produce a single successful quit attempt is less than the average loss per person per smoking year nationally. Given the large healthcare costs and loss of man hours due to tobacco use in the U.S. Navy, increasing smoking cessation treatment options to include varenicline allows for a higher success rate overall.

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